

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

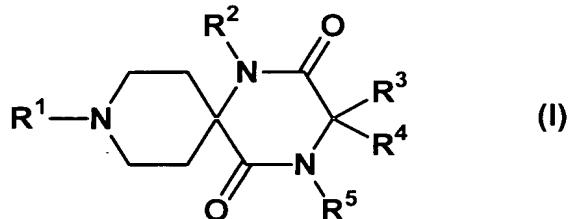
1. **(Currently Amended)** A method for inhibiting function inhibitor of an effector cell, which comprises administering to a mammal an effective amount of a CCR5 antagonist.
2. **(Currently Amended)** The function inhibitor of an effector cell-method according to claim 1, wherein the function is cell migration, cell proliferation or cell activation.
3. **(Currently Amended)** The function inhibitor of an effector cell-method according to claim 1, wherein the effector cell is a CCR5-positive effector cell.
4. **(Currently Amended)** The function inhibitor of an effector cell-method according to claim 1, which is an agent useful for prevention and/or treatment of a disease caused by effector cell function.
5. **(Currently Amended)** The function inhibitor of an effector cell-method according to claim 1, which is an agent useful for prevention and/or treatment of a T cell-mediated disease.
6. **(Currently Amended)** The function inhibitor of an effector cell-method according to claim 1, which is an agent useful for prevention and/or treatment of a myeloid cell-mediated disease.
7. **(Currently Amended)** The function inhibitor of an effector cell-method according to claim 5, wherein the T cell-mediated disease is transplant rejection, autoimmune disease, allergic disease or ischemic disease.
8. **(Currently Amended)** The function inhibitor of an effector cell-method according to claim 6, wherein the myeloid cell-mediated disease is cancer or cancer metastasis.

9. (Currently Amended) The function inhibitor of an effector cell method

according to claim 1, wherein the CCR5 antagonist is a non-peptide substance.

10. (Currently Amended) The function inhibitor of an effector cell method

according to claim 1, wherein the CCR5 antagonist is a compound of formula (I)



wherein R¹ represents (1) a hydrogen atom, (2) C1-18 alkyl, (3) C2-18 alkenyl, (4) C2-18 alkynyl, (5) -COR⁶, (6) -CONR⁷R⁸, (7) -COOR⁹, (8) -SO₂R¹⁰, (9) -COCOOR¹¹, (10) -CONR¹²COR¹³, (11) Cyc1 or (12) C1-18 alkyl, C2-18 alkenyl or C2-18 alkynyl substituted with 1-5 substituent(s) selected from (a) halogen, (b) -CONR⁷R⁸, (c) -COOR⁹, (d) -OR¹⁴, (e) -SR¹⁵, (f) -NR¹⁶R¹⁷, (g) -NR¹⁸COR¹⁹, (h) -SO₂NR²⁰R²¹, (i) -OCOR²², (j) -NR²³SO₂R²⁴, (k) -NR²⁵COOR²⁶, (l) -NR²⁷CONR²⁸R²⁹, (m) Cyc1, (n) keto and (o) -N(SO₂R²⁴)₂;

R⁶-R⁹, R¹¹-R²¹, R²³, R²⁵ and R²⁷-R²⁹ each independently represents (1) a hydrogen atom, (2) C1-8 alkyl, (3) C2-8 alkenyl, (4) C2-8 alkynyl, (5) Cyc1 or (6) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with 1-5 substituent(s) selected from (a) Cyc1, (b) halogen, (c) -OR³⁰, (d) -SR³¹, (e) -NR³²R³³, (f) -COOR³⁴, (g) -CONR³⁵R³⁶, (h) -NR³⁷COR³⁸, (i) -NR³⁹SO₂R⁴⁰ and (j) -N(SO₂R⁴⁰)₂, or

R⁷ and R⁸, R²⁰ and R²¹, or R²⁸ and R²⁹ are taken together to represent (1) C2-6 alkylene, (2) -(C2-6 alkylene)-O-(C2-6 alkylene)-, (3) -(C2-6 alkylene)-S-(C2-6 alkylene)- or (4) -(C2-6 alkylene)-NR¹⁹⁵-(C2-6 alkylene)-, wherein R¹⁹⁵ is a hydrogen atom, C1-8 alkyl, phenyl, or C1-8 alkyl substituted with phenyl;

R¹⁰, R²², R²⁴ and R²⁶ each independently represents (1) C1-8 alkyl, (2) C2-8 alkenyl, (3) C2-8 alkynyl, (4) Cyc1 or (5) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with 1-5

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substituent(s) selected from (a) Cyc1, (b) halogen, (c) -OR³⁰, (d) -SR³¹, (e) -NR³²R³³, (f) -COOR³⁴, (g) -CONR³⁵R³⁶, (h) -NR³⁷COR³⁸, (i) -NR³⁹SO₂R⁴⁰ and (j) -N(SO₂R⁴⁰)₂;
R³⁰-R³⁷ and R³⁹ each independently represents a hydrogen atom, C1-8 alkyl, Cyc1 or C1-8 alkyl substituted with Cyc1, or

R³⁵ and R³⁶ are taken together to represent (1) C2-6 alkylene, (2) -(C2-6 alkylene)-O-(C2-6 alkylene)-, (3) -(C2-6 alkylene)-S-(C2-6 alkylene)- or (4) -(C2-6 alkylene)-NR¹⁹⁶-(C2-6 alkylene)-, wherein R¹⁹⁶ represents a hydrogen atom, C1-8 alkyl, phenyl or C1-8 alkyl substituted with phenyl;

R³⁸ and R⁴⁰ each independently represents C1-8 alkyl, Cyc1 or C1-8 alkyl substituted with Cyc1;

Cyc1 represents a C3-15 mono-, bi- or tri-(fused or spiro)carbocyclic ring or a 3-15 membered mono-, bi- or tri-(fused or spiro)cyclic hetero ring containing 1-4 nitrogen atom(s), 1-3 oxygen atom(s) and/or 1-3 sulfur atom(s), and Cyc1 may be substituted with 1-5 of R⁵¹;

R⁵¹ represents (1) C1-8 alkyl, (2) C2-8 alkenyl, (3) C2-8 alkynyl, (4) halogen, (5) nitro, (6) trifluoromethyl, (7) trifluoromethoxy, (8) nitrile, (9) keto, (10) Cyc2, (11) -OR⁵², (12) -SR⁵³, (13) -NR⁵⁴R⁵⁵, (14) -COOR⁵⁶, (15) -CONR⁵⁷R⁵⁸, (16) -NR⁵⁹COR⁶⁰, (17) -SO₂NR⁶¹R⁶², (18) -OCOR⁶³, (19) -NR⁶⁴SO₂R⁶⁵, (20) -NR⁶⁶COOR⁶⁷, (21) -NR⁶⁸CONR⁶⁹R⁷⁰, (22) -B(OR⁷¹)₂, (23) -SO₂R⁷², (24) -N(SO₂R⁷²)₂, or (25) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with 1-5 substituent(s) selected from (a) halogen, (b) Cyc2, (c) -OR⁵², (d) -SR⁵³, (e) -NR⁵⁴R⁵⁵, (f) -COOR⁵⁶, (g) -CONR⁵⁷R⁵⁸, (h) -NR⁵⁹COR⁶⁰, (i) -SO₂NR⁶¹R⁶², (j) -OCOR⁶³, (k) -NR⁶⁴SO₂R⁶⁵, (l) -NR⁶⁶COOR⁶⁷, (m) -NR⁶⁸CONR⁶⁹R⁷⁰, (n) -B(OR⁷¹)₂, (o) -SO₂R⁷² and (p) -N(SO₂R⁷²)₂;

R⁵²-R⁶², R⁶⁴, R⁶⁶ and R⁶⁸-R⁷¹ each independently represents (1) a hydrogen atom, (2) C1-8 alkyl, (3) C2-8 alkenyl, (4) C2-8 alkynyl, (5) Cyc2 or (6) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with Cyc2, -OR⁷³, -COOR⁷⁴ or -NR⁷⁵R⁷⁶, or

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R^{57} and R^{58} , R^{61} and R^{62} , or R^{69} and R^{70} are taken together to represent (1) C2-6 alkylene, (2) -(C2-6 alkylene)-O-(C2-6 alkylene)-, (3) -(C2-6 alkylene)-S-(C2-6 alkylene)- or (4) -(C2-6 alkylene)-NR¹⁹⁷-(C2-6 alkylene)-, wherein R^{197} represents a hydrogen atom, C1-8 alkyl, phenyl or C1-8 alkyl substituted with phenyl;

R^{63} , R^{65} , R^{67} and R^{72} each independently represents (1) C1-8 alkyl, (2) C2-8 alkenyl, (3) C2-8 alkynyl, (4) Cyc2 or (5) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with Cyc2, -OR⁷³, -COOR⁷⁴ or -NR⁷⁵R⁷⁶;

R^{73} - R^{76} each independently represents a hydrogen atom, C1-8 alkyl, Cyc2 or C1-8 alkyl substituted with Cyc2;

Cyc2 has the same meaning as Cyc1, and Cyc2 may be substituted with 1-5 of R^{77} ; R^{77} represents (1) C1-8 alkyl, (2) halogen, (3) nitro, (4) trifluoromethyl, (5) trifluoromethoxy, (6) nitrile, (7) -OR⁷⁸, (8) -NR⁷⁹R⁸⁰, (9) -COOR⁸¹, (10) -SR⁸², (11) -CONR⁸³R⁸⁴, (12) C2-8 alkenyl, (13) C2-8 alkynyl, (14) keto, (15) Cyc6, (16) -NR¹⁶¹COR¹⁶², (17) -SO₂NR¹⁶³R¹⁶⁴, (18) -OCOR¹⁶⁵, (19) -NR¹⁶⁶SO₂R¹⁶⁷, (20) -NR¹⁶⁸COOR¹⁶⁹, (21) -NR¹⁷⁰CONR¹⁷¹R¹⁷², (22) -SO₂R¹⁷³, (23) -N(SO₂R¹⁶⁷)₂ or (24) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with 1-5 substituent(s) selected from (a) halogen, (b) -OR⁷⁸, (c) -NR⁷⁹R⁸⁰, (d) -COOR⁸¹, (e) -SR⁸², (f) -CONR⁸³R⁸⁴, (g) keto, (h) Cyc6, (i) -NR¹⁶¹COR¹⁶², (j) -SO₂NR¹⁶³R¹⁶⁴, (k) -OCOR¹⁶⁵, (l) -NR¹⁶⁶SO₂R¹⁶⁷, (m) -NR¹⁶⁸COOR¹⁶⁹, (n) -NR¹⁷⁰CONR¹⁷¹R¹⁷², (o) -SO₂R¹⁷³, and (p) -N(SO₂R¹⁶⁷)₂;

R^{78} - R^{84} , R^{161} - R^{164} , R^{166} , R^{168} and R^{170} - R^{172} each independently represents (a) a hydrogen atom, (b) C1-8 alkyl, (c) C2-8 alkenyl, (d) C2-8 alkynyl, (e) Cyc6, (f) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with Cyc6, -OR¹⁷⁴, -COOR¹⁷⁵, -NR¹⁷⁶R¹⁷⁷ or -CONR¹⁷⁸R¹⁷⁹, or

R^{83} and R^{84} , R^{163} and R^{164} , or R^{171} and R^{172} are taken together to represent (1) C2-6 alkylene, (2) -(C2-6 alkylene)-O-(C2-6 alkylene)-, (3) -(C2-6 alkylene)-S-(C2-6 alkylene)- or (4)

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-(C2-6 alkylene)-NR¹⁹⁸-(C2-6 alkylene)-, wherein R¹⁹⁸ represents a hydrogen atom, C1-8 alkyl, phenyl or C1-8 alkyl substituted with phenyl;

R¹⁶⁵, R¹⁶⁷, R¹⁶⁹ and R¹⁷³ each independently represents (a) C1-8 alkyl, (b) C2-8 alkenyl, (c) C2-8 alkynyl, (d) Cyc6 or (e) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with Cyc6, -OR¹⁷⁴, -COOR¹⁷⁵, -NR¹⁷⁶R¹⁷⁷ or -CONR¹⁷⁸R¹⁷⁹;

R¹⁷⁴-R¹⁷⁷ each independently represents (1) a hydrogen atom, (2) C1-8 alkyl, (3) Cyc6 or (4) C1-8 alkyl substituted with Cyc6, or

R¹⁷⁸ and R¹⁷⁹ are taken together to represent (1) C2-6 alkylene, (2) -(C2-6 alkylene)-O-(C2-6 alkylene)-, (3) -(C2-6 alkylene)-S-(C2-6 alkylene)- or (4) -(C2-6 alkylene)-NR¹⁹⁹-(C2-6 alkylene)-, wherein R¹⁹⁹ represents a hydrogen atom, C1-8 alkyl, phenyl or C1-8 alkyl substituted with phenyl;

Cyc6 represents a C3-8 mono-carbocyclic ring or a 3-8 membered mono-cyclic hetero ring containing 1-4 nitrogen atom(s), 1-2 oxygen atom(s) and/or 1-2 sulfur atom(s), with the proviso that, Cyc6 may be substituted with 1-5 of R¹⁸⁰;

R¹⁸⁰ represents (1) C1-8 alkyl, (2) halogen, (3) nitro, (4) trifluoromethyl, (5) trifluoromethoxy, (6) nitrile, (7) -OR¹⁸¹, (8) -NR¹⁸²R¹⁸³, (9) -COOR¹⁸⁴, (10) -SR¹⁸⁵ or (11) -CONR¹⁸⁶R¹⁸⁷;

R¹⁸¹-R¹⁸⁷ each independently represents (1) a hydrogen atom, (2) C1-8 alkyl, (3) phenyl or (4) C1-8 alkyl substituted with phenyl, or

R¹⁸² and R¹⁸³, or R¹⁸⁶ and R¹⁸⁷ are taken together to represent (1) C2-6 alkylene, (2) -(C2-6 alkylene)-O-(C2-6 alkylene)-, (3) -(C2-6 alkylene)-S-(C2-6 alkylene)- or (4) -(C2-6 alkylene)-NR²⁰⁰-(C2-6 alkylene)-, wherein R²⁰⁰ represents a hydrogen atom, C1-8 alkyl, phenyl, C1-8 alkyl substituted with phenyl;

R² represents (1) a hydrogen atom, (2) C1-8 alkyl, (3) C2-8 alkenyl, (4) C2-8 alkynyl, (5) -OR⁹⁰, (6) Cyc3 or (7) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with 1-5

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substituent(s) selected from (a) halogen, (b) -OR⁹⁰, (c) -SR⁹¹, (d) -NR⁹²R⁹³, (e) -COOR⁹⁴, (f) -CONR⁹⁵R⁹⁶, (g) -NR⁹⁷COR⁹⁸, (h) -SO₂NR⁹⁹R¹⁰⁰, (i) -OCOR¹⁰¹, (j) -NR¹⁰²SO₂R¹⁰³, (k) -NR¹⁰⁴COOR¹⁰⁵, (l) -NR¹⁰⁶CONR¹⁰⁷R¹⁰⁸, (m) Cyc3, (n) keto and (o) -N(SO₂R¹⁰³)₂;
R⁹⁰-R¹⁰⁰, R¹⁰², R¹⁰⁴ and R¹⁰⁶-R¹⁰⁸ each independently represents (1) a hydrogen atom, (2) C1-8 alkyl, (3) C2-8 alkenyl, (4) C2-8 alkynyl, (5) Cyc3 or (6) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with Cyc3, or

R⁹⁵ and R⁹⁶, R⁹⁹ and R¹⁰⁰, or R¹⁰⁷ and R¹⁰⁸ are taken together to represent (1) C2-6 alkylene, (2) -(C2-6 alkylene)-O-(C2-6 alkylene)-, (3) -(C2-6 alkylene)-S-(C2-6 alkylene)- or (4) -(C2-6 alkylene)-NR²⁰¹-(C2-6 alkylene)-, wherein R²⁰¹ is a hydrogen atom, C1-8 alkyl, phenyl or C1-8 alkyl substituted with phenyl;

R¹⁰¹, R¹⁰³ and R¹⁰⁵ are each independently (1) C1-8 alkyl, (2) C2-8 alkenyl, (3) C2-8 alkynyl or (4) Cyc3, or C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with Cyc3;

Cyc3 has the same meaning as Cyc1, and Cyc3 may be substituted with 1-5 of R¹⁰⁹;

R¹⁰⁹ has the same meaning as R⁵¹;

R³ and R⁴ each independently represents (1) a hydrogen atom, (2) C1-8 alkyl, (3) C2-8 alkenyl, (4) C2-8 alkynyl, (5) -COOR¹²⁰, (6) -CONR¹²¹R¹²², (7) Cyc4 or (8) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with 1-5 substituent(s) selected from (a) halogen, (b) nitrile, (c) Cyc4, (d) -COOR¹²⁰, (e) -CONR¹²¹R¹²², (f) -OR¹²³, (g) -SR¹²⁴, (h) -NR¹²⁵R¹²⁶, (i) -NR¹²⁷COR¹²⁸, (j) -SO₂NR¹²⁹R¹³⁰, (k) -OCOR¹³¹, (l) -NR¹³²SO₂R¹³³, (m) -NR¹³⁴COOR¹³⁵, (n) -NR¹³⁶CONR¹³⁷R¹³⁸, (o) -S-SR¹³⁹, (p) -NHC(=NH)NHR¹⁴⁰, (q) keto, (r) -NR¹⁴⁵CONR¹⁴⁶COR¹⁴⁷ and (s) -N(SO₂R¹³³)₂;

R¹²⁰-R¹³⁰, R¹³², R¹³⁴, R¹³⁶-R¹³⁸, R¹⁴⁵ and R¹⁴⁶ each independently represents (1) a hydrogen atom, (2) C1-8 alkyl, (3) C2-8 alkenyl, (4) C2-8 alkynyl, (5) Cyc4 or (6) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with Cyc4, halogen, -OR¹⁴⁸, -SR¹⁴⁹, -COOR¹⁵⁰ or -NHCOR¹⁴¹, or

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R^{121} and R^{122} , R^{129} and R^{130} , or R^{137} and R^{138} are taken together to represent (1) C2-6 alkylene, (2) -(C2-6 alkylene)-O-(C2-6 alkylene)-, (3) -(C2-6 alkylene)-S-(C2-6 alkylene)- or (4) -(C2-6 alkylene)-NR²⁰¹-(C2-6 alkylene)-, wherein R^{201} represents a hydrogen atom, C1-8 alkyl, phenyl, C1-8 alkyl substituted with phenyl;

R^{131} , R^{133} , R^{135} , R^{139} and R^{147} each independently represents (1) C1-8 alkyl, (2) C2-8 alkenyl, (3) C2-8 alkynyl, (4) Cyc4 or (5) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with Cyc4, halogen, -OR¹⁴⁸, -SR¹⁴⁹, -COOR¹⁵⁰ or -NHCOR¹⁴¹,

R^{140} represents a hydrogen atom, -COOR¹⁴² or -SO₂R¹⁴³;

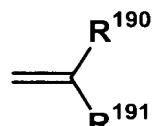
R^{141} - R^{143} each independently represents (1) C1-8 alkyl, (2) C2-8 alkenyl, (3) C2-8 alkynyl, (4) Cyc4 or (5) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with Cyc4;

R^{148} - R^{150} each independently represents (1) a hydrogen atom, (2) C1-8 alkyl, (3) C2-8 alkenyl, (4) C2-8 alkynyl, (5) Cyc4 or (6) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with Cyc4;

Cyc4 has the same meaning as Cyc1, and Cyc4 may be substituted with 1-5 of R^{144} ;

R^{144} has the same meaning as R^{51} , or

R^3 and R^4 are taken together to represent



wherein R^{190} and R^{191} each independently represents (1) a hydrogen atom, (2) C1-8 alkyl, (3) C2-8 alkenyl, (4) C2-8 alkynyl, (5) -COOR¹²⁰, (6) -CONR¹²¹ R^{122} , (7) Cyc4 or (8) C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with 1-5 substituent(s) selected from (a) halogen, (b) nitrile, (c) Cyc4, (d) -COOR¹²⁰, (e) -CONR¹²¹ R^{122} , (f) -OR¹²³, (g) -SR¹²⁴, (h) -NR¹²⁵ R^{126} , (i) -NR¹²⁷COR¹²⁸, (j) -SO₂NR¹²⁹ R^{130} , (k) -OCOR¹³¹, (l) -NR¹³²SO₂R¹³³, (m) -NR¹³⁴COOR¹³⁵, (n) -

NR¹³⁶CONR¹³⁷R¹³⁸, (o) -S-SR¹³⁹, (p) -NHC(=NH)NHR¹⁴⁰, (q) keto, (r) -NR¹⁴⁵CONR¹⁴⁶COR¹⁴⁷ and (s) -N(SO₂R¹³³)₂;

R¹²⁰-R¹⁴⁰ and R¹⁴⁵-R¹⁴⁷ have the same meanings as described above;

R⁵ represents (1) a hydrogen atom, (2) C1-8 alkyl, (3) Cyc5 or (4) C1-8 alkyl substituted with Cyc5;

Cyc5 has the same meaning as Cyc1, and Cyc5 may be substituted with 1-5 of R¹⁵⁰;

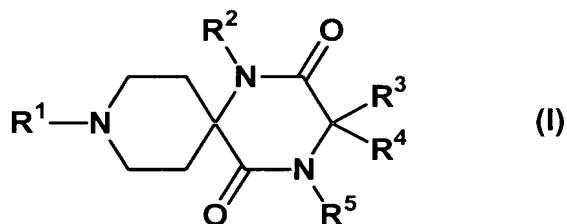
R¹⁵⁰ has the same meaning as R⁵¹;

an N-oxide thereof, a salt thereof, or a prodrug thereof.

11. **(Original)** A medicament which comprises a function inhibitor of an effector cell comprising a CCR5 antagonist, in combination with one, two or more immunosuppressive drug(s).

12. **(Original)** The medicament according to claim 11, wherein the one, two or more immunosuppressive drug(s) are selected from the group of tacrolimus, cyclosporine, sirolimus, corticosteroid, azathioprine, mycophenolate mofetil, FTY-720 and cyclophosphamide.

13. **(Currently Amended)** ~~A method for prevention and/or treatment of a disease caused by effector cell function, which comprises administering to a mammal an effective amount of~~ The medicament according to claim 11, wherein the CCR5 antagonist is a compound of formula (I)



wherein all symbols have the same meanings as those defined in claim 10, an N-oxide thereof, a salt thereof, or a prodrug thereof.

Claim 14. **(Cancelled)**